WO 2005/005630 PCT/EP2004/007606

57

CLAIMS

- An isolated nucleic acid molecule comprising a nucleotide sequence encoding a (poly)peptide having LPI
 activity, said nucleotide sequence corresponding to a sequence being selected from the group consisting of:
 - a) a nucleotide sequence comprising a part of one of the sequences as depicted in Figure 2a and 2b and identified as SEQ ID NO:2; SEQ ID NO:4; SEQ ID NO:6);
- b) nucleotide sequences encoding a (poly)peptide having LPI activity and having the amino acid sequence depicted in Figure 3 and identified as SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7;
- c) nucleotide sequences encoding a (poly)peptide

 15 having LPI activity and having a portion of the amino acid
 sequence depicted in Figure 3 identified as SEQ ID NO:3, SEQ

 ID NO:5 or SEQ ID NO:7;
 - d) nucleotide sequences being at least 40% identical to any one of the nucleotide sequences a), b) or c);
- e) nucleotide sequences hybridizing at stringent conditions with any one of the nucleotide sequences a), b), c) or d), and
 - f) nucleotide sequences complementary to any of the nucleotide sequences a), b), c), d) or e).
- 2. An isolated nucleic acid molecule as claimed in claim 1, of which the part of the nucleotide sequence as defined in claim 1 under a) corresponds to nucleotides 1 to 490 of Figure 2a (SEQ ID NO:2).
- 3. An isolated nucleic acid molecule as claimed in claim 1 or 2, of which the part of the nucleotide sequence as defined in claim 1 under a) corresponds to nucleotides 41 to 490 of Figure 2a (SEQ ID NO:2).

- 4. An isolated nucleic acid molecule as claimed in claim 1, 2 or 3, of which the part of the nucleotide sequence as defined in claim 1 under a) corresponds to nucleotides 125 to 490 of Figure 2a (SEQ ID NO:2).
- 5. An isolated nucleic acid molecule as claimed in claim 1, of which the part of the nucleotide sequence as defined in claim 1 under a) corresponds to nucleotides 1 to 490 of lpi-B (SEQ ID NO:4) or lpi-C (SEQ ID NO:6) in Figure 2b.
- 6. An isolated nucleic acid molecule as claimed in claim 1 or 2, of which the part of the nucleotide sequence as defined in claim 1 under a) corresponds to nucleotides 41 to 490 of lpi-B (SEQ ID NO:4) or lpi-C (SEQ ID NO:6) in Figure 2b.
- 7. An isolated nucleic acid molecule as claimed in claim 1, 2 or 3, of which the part of the nucleotide sequence as defined in claim 1 under a) corresponds to nucleotides 125 to 490 of lpi-B (SEQ ID NO:4) or lpi-C (SEQ ID NO:6) in Figure 2b.
- 8. An isolated nucleic acid molecule as claimed in claims 1-7, wherein the nucleotide sequence as defined in claim 1 under d) is at least 40%, at least 50%, preferably at least 60% or at least 70%, more preferably at least 75%, even more preferably at least 80%, most preferably at least 90% identical to any one of the nucleotide sequences a), b) or c).
- 9. An isolated nucleic acid molecule as claimed in claims 1-8, wherein the stringent conditions are constituted by overnight hybridization at 42°C in 5xSSC and washing at 30 65°C at 0.1xSSC.
 - 10. An isolated nucleic acid molecule as claimed in claims 1-9, wherein a portion of the amino acid sequence as defined in claim 1 under c) constitutes alone or with other

portions of the amino acid sequence the region(s) of the (poly)peptide having LPI activity that lead to biological activity.

- 11. An isolated nucleic acid molecule as claimed in 5 claims 1-10, which nucleic acid is DNA, RNA or cDNA.
 - 12. Recombinant vector comprising an isolated nucleic acid molecule as claimed in claims 1-11.
- 13. Method for making a recombinant vector comprising inserting at least one isolated nucleic acid molecule as10 claimed in claims 1-11 into a vector.
 - 14. Bacteriophage comprising an isolated nucleic acid molecule as claimed in claims 1-11.
- 15. Recombinant host cell or organism comprising an isolated nucleic acid molecule as claimed in claims 1-11, a vector as claimed in claim 12 or a bacteriophage as claimed in claim 14.
- 16. A recombinant host cell as claimed in claim
 15, wherein the host cell is selected from the group
 consisting of the bacteria Escherichia coli, Bacillus
 20 subtilis, Staphylococcus aureus, the yeasts Saccharomyces
 cerevisiae, Pichia pastoris, Candida, insect cells of the
 Drosophila system and the Baculovirus system, the mammalian
 cells monkey COS, hamster CHO, hamster BHK, hamster RBL-2H3,
 human 293, human 3T3, human HeLa, human U937, human HL-60,
 25 human Jurkat cells, mouse L cells.
 - 17. Method for producing a recombinant (poly)peptide having LPI activity, comprising culturing a recombinant host of claim 15 or 16 under conditions such that said (poly)peptide is expressed and recovering said (poly)peptide.
- 30 18. Method as claimed in claim 17, wherein the host cell is an *Escherichia coli* cell.
 - 19. Method as claimed in claim 17, wherein the host cell is a Staphylococcus aureus cell.

- 20. Method as claimed in claim 19, wherein the Staphylococcus aureus cell is from a strain that already produces an endogenous protein having LPI activity (LPI).
- 21. Method for producing a synthetic (poly)peptide
 5 having LPI activity, comprising deducing the amino acid
 sequence encoded by a nucleic acid molecule as claimed in
 claims 1-11 and synthetically producing a (poly)peptide
 having the said amino acid sequence.
- 22. (Poly)peptide having LPI activity obtainable by 10 any one of the methods as claimed in claims 17-21.
 - 23. (Poly)peptide as claimed in claim 22 for use in diagnosis, prophylaxis or therapy.
- 24. (Poly)peptide as claimed in claim 22 or 23 for use in the treatment of acute and chronic inflammation 15 reactions.
 - 25. (Poly)peptide as claimed in claim 22 or 23 for use in the treatment diseases in **Table 2**.
- 26. Use of the (poly)peptide as claimed in claim 22 for the manufacture of a therapeutic preparation for 20 diagnosis, prophylaxis or therapy.
 - 27. Use as claimed in claim 26 for the treatment of acute and chronic inflammation reactions.
 - 28. Use as claimed in claims 26 or 27 for the treatment of diseases in **Table 2**.
- 29. A therapeutic composition comprising a suitable excipient and the (poly)peptide as claimed in claim 22.
 - 30. A composition as claimed in claim 29 for treating acute and chronic inflammation reactions as listed in Table 2.
- 30 31. A composition as claimed in claim 29 for treating diseases in Table 2.

WO 2005/005630 PCT/EP2004/007606

61

- 32. An antibody or biologically active fragment thereof specifically directed to the (poly)peptide as claimed in claim 22.
- 33. An antibody as claimed in claim 32 for use in 5 diagnosis, prophylaxis or therapy.
 - 34. An antibody as claimed in claim 32 or 33 for use in the treatment of staphylococcus infection.
- 35. Use of an antibody as claimed in claim 32 for the manufacture of a therapeutic preparation for diagnosis,10 prophylaxis or therapy.
 - 36. Use as claimed in claim 35 for the treatment of staphylococcus infection.
- 37. Therapeutic composition comprising a suitable excipient and one or more antibodies as claimed in claim 32 and/or biologically active fragments thereof.
 - 38. An isolated nucleic acid molecule for use in gene therapy.
 - 39. Method for treating a subject suffering from inflammation by administering a therapeutically effective amount of a (poly)peptide as claimed in claim 22.

20

- 40. Method for gene therapeutically treating a subject suffering from inflammation by administering a therapeutically effective amount of a nucleic acid molecule as claimed in claims 1-11.
- 25 41. Method for treating a subject suffering from staphylococcus infection by administering a therapeutically effective amount of an antibody and/or biologically active fragment thereof as claimed in claim 32.
- 42. Method for isolating from an organism a gene
 30 encoding a protein having LPI activity, comprising screening
 of a genomic or cDNA library of that organism with a probe
 based on the nucleic acid molecule as claimed in claims 1-11,

WO 2005/005630 PCT/EP2004/007606

isolation of the positive clones, and testing whether the positive clones show LPI activity.

- 43. Method for identifying nucleic acid sequences encoding a (poly)peptide having LPI activity, comprising comparison of the sequence as depicted in Figures 2a and 2b identified by SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6 with the nucleic acid or protein sequence information contained in a database and selecting sequences that are at least 60% identical to the sequences as depicted in Figures 2a and 2b and identified by SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6.
- 44. Method for identifying amino acid sequences of a (poly)peptide having LPI activity, comprising comparison of the sequences as depicted in Figure 3 and identified by SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 with the nucleic acid or protein sequence information contained in a database and selecting sequences that are at least 40% identical to the sequences as depicted in Figure 3 and identified by SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7.
- 45. Micro-organism harboring a nucleic acid molecule
 20 as claimed in claims 1-11 for use as a medicament for the
 treatment of acute and chronic inflammation reactions.
 - 46. Micro-organism as claimed in claim 42 for treating diseases listed in **Table 2**.
- 47. Method for producing (poly)peptide(s) having LPI activity, comprising culturing wild-type, non-recombinant, Staphylococcus strains that produce endogenous priming/activation inhibitory (poly)peptide(s) and recovering same.
- 48. (Poly)peptide having an amino acid sequence that is at least 40% homologous to the amino acid sequence

 30 depicted in Figure 3 (SEQ ID NO:3; SEQ ID NO:5; SEQ ID NO:7) and having at least LPI activity.